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| 10/712,763 | 11/12/2003 | Barry James Maurer | 54652.8013.US00 | 7398 |

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PERKINS COIE LLP
POST OFFICE BOX 1208
SEATTLE, WA 98111-1208

| EXAMINER | |
|---|---|
| ANDERSON, JAMES D | |
| **ART UNIT** | **PAPER NUMBER** |
| 1614 | |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/712,763 | MAURER ET AL. | |
| | Examiner | Art Unit | |
| | James D. Anderson | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *30 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *12-14,21-23,33 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-14,21-23,33 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**CLAIMS 12-14, 21-23 & 33-34 ARE PRESENTED FOR EXAMINATION**

Applicants' amendment filed 3/30/2007 has been received and entered into the application. Accordingly, claims 12-13 and 21-22 have been amended, claims 1-11, 15-20 and 24-32 have been cancelled and claims 33-34 have been added.

In view of the above amendments, the objection to claims 13, 22, 25 and 27 has been overcome and thus is *withdrawn*. Also, the amendments and Applicants' remarks have overcome the rejections not reiterated herein from the previous office action. Such rejections are hereby *withdrawn*. The following rejections are either reiterated or newly applied and constitute the totality of issues remaining in the present application.

In light of the new rejections being applied against the pending claims, this Office Action is **Non-Final**.

***Oath/Declaration***

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
It does not identify the citizenship of each inventor.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 12-14, 21-23, 33 and 34 are rejected under 35 U.S.C. § 102(b) as being anticipated by Maurer *et al.* (U.S. Patent No. 6,352,844; Issued March 5, 2002) (prior art of record).

Applicants argue that their amendments render the present rejection moot. The Examiner is not persuaded that Maurer *et al.* do not anticipate the present claims. In addition, upon further consideration claims 13-14 and 22-23 are added to the present rejection as also being anticipated by Maurer *et al.* Applicants' added limitation wherein the claimed methods do not comprise administration of L-threo-PPMP are anticipated by Maurer *et al.* because the reference teaches that functional homologues, isomers, and salts of glucosylceramide synthesis inhibitors (including PPMP) are useful compounds of the invention (col. 10, lines 14-15). As such, Maurer *et al.* reasonably anticipates administration of the individual enantiomers because "isomers" is reasonably interpreted to include stereoisomerism as well as structural isomerism.

Maurer *et al.* teach methods of treating hyperproliferative disorders comprising administration of: a) a ceramide-generating retinoid; and b) a ceramide-degradation inhibitor (Abstract; Claims). Said ceramide-generating retinoid is preferably fenretinide or a pharmaceutically acceptable salt thereof (col. 9, lines 16-25; Claims 4, 7, 11 and 14). Said ceramide-degradation inhibitor can be a glucosylceramide synthesis inhibitor, including 1-phenyl-2-palmitoylamino-3-morphilino-1-propanol (PPMP) (col. 9, line 61 to col. 10, line 28). Functional homologues, isomers, and salts thereof are taught to be useful compounds of the invention (col. 10, lines 14-15) thus reasonably encompassing the instantly claimed D-threo-PPMP enantiomer. Inhibition of 1-O-acylceramide synthase as required in instant claims 33 and

34 would be inherent in the methods disclosed in Maurer *et al.* when PPMP is administered as the ceramide-degradation inhibitor. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). Further, instant claims wherein the ceramide degradation inhibitor "comprises D-threo-PPMP" are anticipated by the reference because the claimed isomer is present in the methods described in Maurer *et al.* The ceramide-generating retinoids are given in amounts effective to produce necrosis, apoptosis, or both in the tumor, and the ceramide-degradation inhibitor is administered in an amount effective to increase necrosis or apoptosis or both in the tumor (Claims). The active compounds described in Maurer *et al.* (namely ceramide-generating retinoids and ceramide-degradation inhibitors) can be formulated for administration in a single pharmaceutical carrier and may be administered orally, topically and intravenously (col. 14, lines 11-15 and 33-42).

Accordingly, the claims are deemed properly rejected as being anticipated by Maurer *et al.* who teach methods of treating hyperproliferative disorders comprising administering fenritinide and PPMP.

Claims 12, 21, 33 and 34 are rejected under 35 U.S.C. § 102(b) as being anticipated by Maurer *et al.* (U.S. Patent No. 6,368,831; Issued April 9, 2002).

Applicants argue that their amendments render the present rejection moot. The Examiner is not persuaded that Maurer *et al.* do not anticipate the present claims. In addition, upon further consideration, claims 13-14 and 22-23 are added to the present rejection as also being anticipated by Maurer *et al.* Applicants' added limitation wherein the claimed methods do not comprise administration of L-threo-PPMP are still anticipated by Maurer *et al.* because the reference

teaches that functional homologues, isomers, and salts of glucosylceramide synthesis inhibitors (including PPMP) are useful compounds of the invention (col. 9, lines 48-49). As such, Maurer *et al.* reasonably anticipates administration of the individual enantiomers because "isomers" is reasonably interpreted to include stereoisomerism as well as structural isomerism.

Maurer *et al.* teach methods of treating hyperproliferative disorders comprising administration of: a) a ceramide-generating retinoid; and b) a ceramide-degradation inhibitor (Abstract; Claims). Said ceramide-generating retinoid is preferably fenretinide or a pharmaceutically acceptable salt thereof (col. 8, lines 51-60; Claims 4, 7, 11, 14 and 25). Said ceramide-degradation inhibitor can be a glucosylceramide synthesis inhibitor and/or 1-acylceramide synthase inhibitor, including 1-phenyl-2-palmitoylamino-3-morphilino-1-propanol (PPMP) and functional homologues, isomers, and salts thereof (col. 9, lines 25-63). PPMP is disclosed to inhibit both glucosylceramide synthesis inhibitor and 1-acylceramide synthase as recited in instant claims 33 and 34 (col. 22, line 59 to col. 23, line 45). The diasteriomer, D,L-threo-PPMP, is taught to inhibit both glucosylceramide synthesis and 1-O-acylceramide synthase and significantly increase the cytotoxicity of fenretinide (col. 23, lines 2-45). Further, instant claims wherein the ceramide degradation inhibitor "*comprises* D-threo-PPMP" are anticipated by the reference because the claimed isomer is present in the methods described in the '831 patent. The ceramide-generating retinoids are given in amounts effective to produce necrosis, apoptosis, or both in the tumor and the ceramide-degradation inhibitor is administered in an amount effective to increase necrosis or apoptosis or both in the tumor (Claims). The active compounds described in Maurer *et al.* (namely ceramide-generating retinoids and ceramide-degradation

inhibitors) can be formulated for administration in a single pharmaceutical carrier and may be administered orally, topically and intravenously (col. 13, lines 34-36 and 54-62).

Accordingly, the claims are deemed properly rejected as being anticipated by Maurer *et al.* who teach methods of treating hyperproliferative disorders comprising administering fenritinide and PPMP.

***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 12-14, 21-23, 33 and 34 are rejected under 35 U.S.C. § 103(a) as being obvious over Maurer *et al.* (U.S. Patent No. 6,368,831; Issued April 9, 2002).

Maurer *et al.* disclose methods and formulations for treating hyperproliferative disorders comprising administration of: a) a ceramide-generating retinoid; and b) a ceramide-degradation inhibitor (Abstract; Claims). Said ceramide-generating retinoid is preferably fenretinide or a pharmaceutically acceptable salt thereof (col. 8, lines 51-60; Claims 4, 7, 11, 14 and 25). Said

ceramide-degradation inhibitor can be a glucosylceramide synthesis inhibitor and/or 1-acylceramide synthase inhibitor, including 1-phenyl-2-palmitoylamino-3-morphilino-1-propanol (PPMP) and functional homologues, isomers, and salts thereof (col. 9, lines 25-63). PPMP is disclosed to inhibit both glucosylceramide synthesis inhibitor and 1-acylceramide synthase (col. 22, line 59 to col. 23, line 45). The diasteriomer, D,L-threo-PPMP, is taught to inhibit both glucosylceramide synthesis and 1-O-acylceramide synthase and significantly increase the cytotoxicity of fenretinide (col. 23, lines 2-45). The ceramide-generating retinoids are given in amounts effective to produce necrosis, apoptosis, or both in the tumor and the ceramide-degradation inhibitor is administered in an amount effective to increase necrosis or apoptosis or both in the tumor (Claims). The active compounds described in the '831 patent (namely ceramide-generating retinoids and ceramide-degradation inhibitors) can be formulated for administration in a single pharmaceutical carrier and may be administered orally, topically and intravenously (col. 13, lines 34-36 and 54-62).

In the absence of a showing of unexpected results commensurate in scope with the claims, the instantly claimed methods and formulations wherein the ceramide degradation inhibitor comprises D-threo-PPMP and wherein L-threo-PPMP is not administered would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. Maurer *et al.* disclose that D,L-threo-PPMP inhibits both glucosylceramide synthesis and 1-O-acylceramide synthase and significantly increases the cytotoxicity of fenretinide (col. 23, lines 2-45). Further, the patent discloses that isomers of the disclosed glucosylceramide synthesis inhibitors and/or 1-acylceramide synthase inhibitors, including 1-phenyl-2-palmitoylamino-3-

morphilino-1-propanol (PPMP) can be used in the invention. In fact, the D enantiomer of such compounds is preferred (col. 9, lines 50-51).

As such, the skilled artisan would be imbued with at least a reasonable expectation that all isomers of D,L-threo-PPMP, and preferably D enantiomers thereof, would be effective in the methods disclosed in Maurer *et al.*

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

U.S. Patent No. 6,368,831

Claims 12-14, 21-23, 33 and 34 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 and 20-23 of U.S. Patent No. 6,368,831. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed methods are encompassed by the methods claimed in the '831 patent. Recitation of a specific enantiomer of PPMP does not patentably distinguish the claimed methods from those of the '831 patent.

U.S. Patent No. 6,352,844

Claims 12-14, 21-23, 33 and 34 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,352,844. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed methods are encompassed by the methods claimed in the '844 patent. Recitation of a specific enantiomer of PPMP does not patentably distinguish the claimed methods from those of the '831 patent.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

James D. Anderson
Patent Examiner
AU 1614

June 14, 2007

Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER

6/15/07